FDA CBER's Recent Initiatives, Policies, and Inspections

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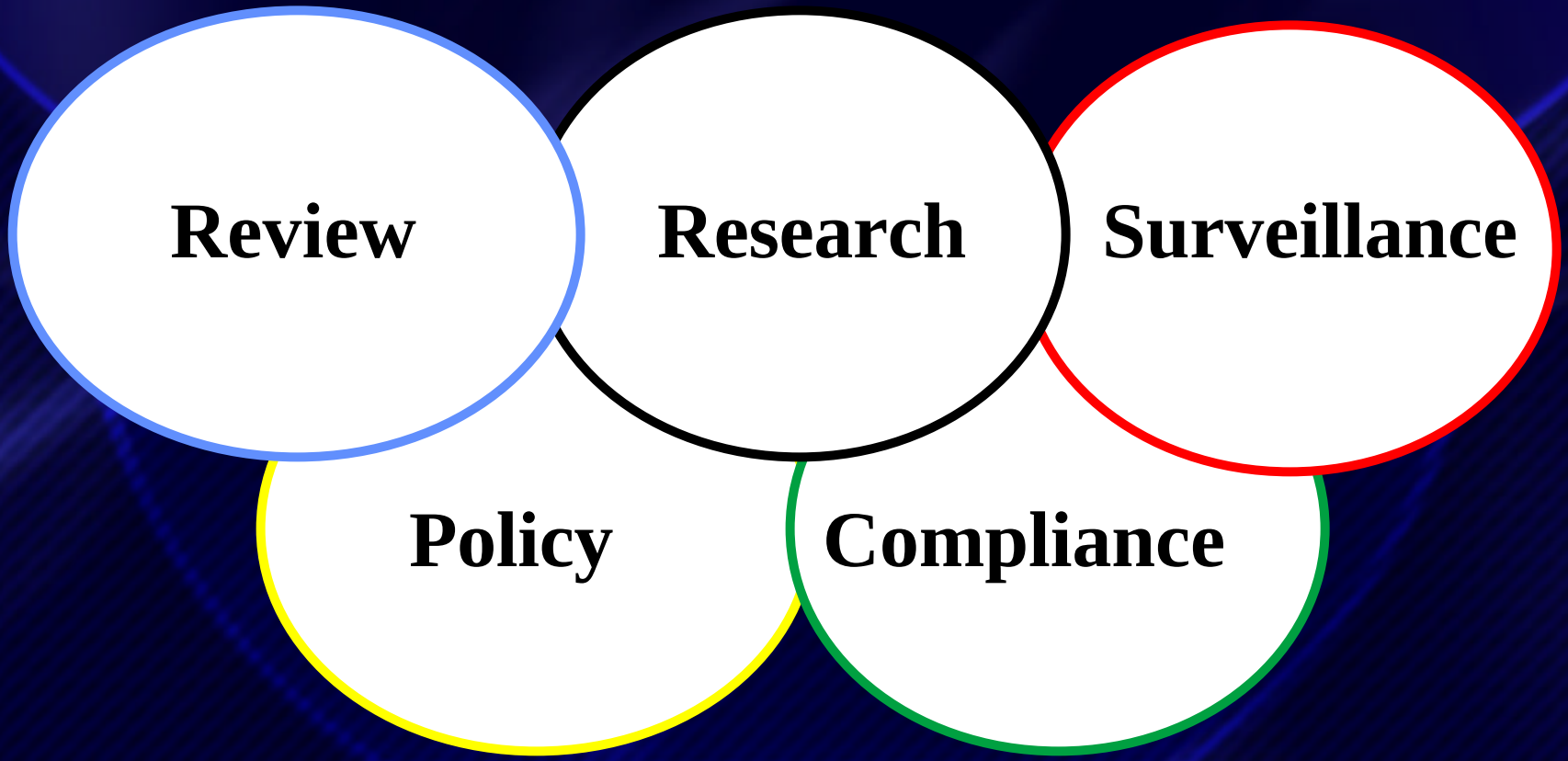
Agenda

- Overview of CBER and Recent Initiatives
- General Differences Between CBER and CDER
- CBER/CDER Therapeutic Product Transfer
- Pharmaceutical CGMPs for the 21st Century: A Risk-Based Approach (including inspections)
- Counter-Terrorism

CBER Regulation

Based on Sound Science, Law, and Public Health Impact

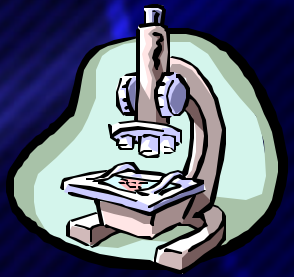


Shepherding Safe and Effective Products

Regulatory Research

FDA

Bench **Bedside** **Marketplace**



Translational Research

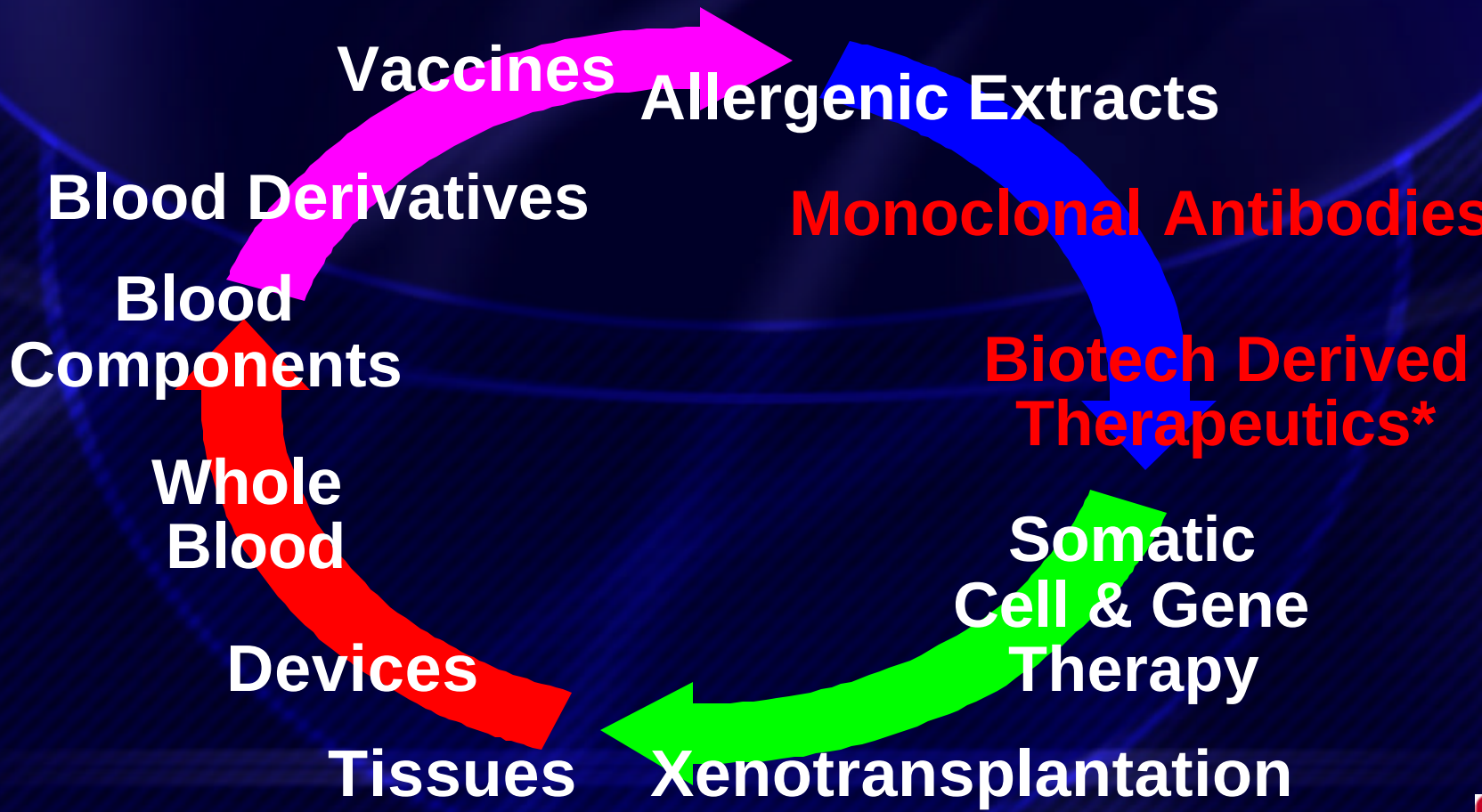
NIH
Academia
Industry

Pharmaceutical Research

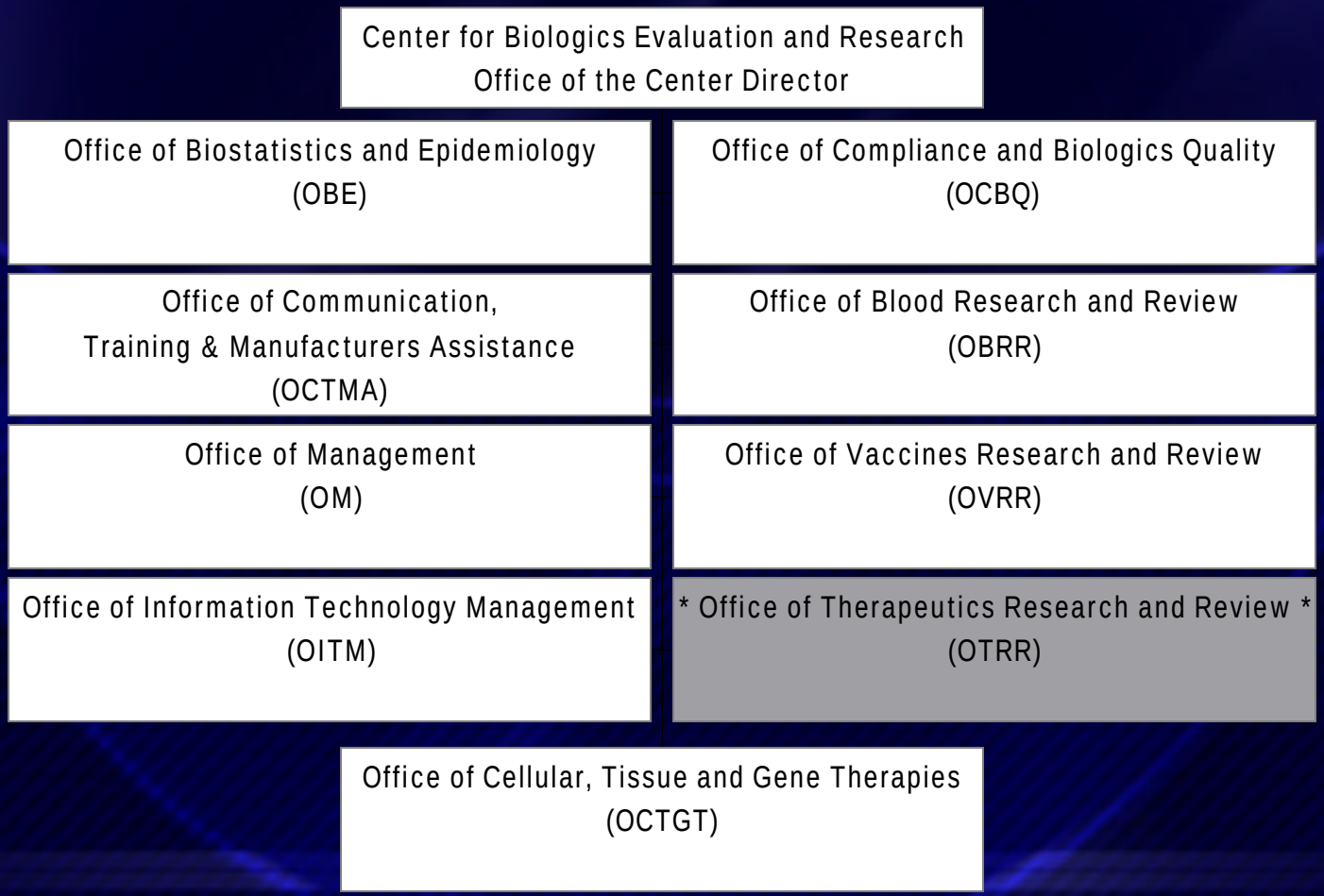
Industry

BASIC **APPLIED** **SAFETY & QUALITY**

Biological Products Regulated by CBER



CBER


Center for Biologics Evaluation and Research
Office of the Center Director
Office of Biostatistics and Epidemiology
(OBE)
Office of Compliance and Biologics Quality
(OCBQ)
Office of Communication,
Training & Manufacturers Assistance
(OCTMA)
Office of Blood Research and Review
(OBRR)
Office of Management
(OM)
Office of Vaccines Research and Review
(OVRR)
Office of Information Technology Management
(OITM)
* Office of Therapeutics Research and Review *
(OTRR)
Office of Cellular, Tissue and Gene Therapies
(OCTGT)

CBER Priority Issues

- Work with CBER staff/leadership to seek internal/external input on CBER science and regulation
- Enhance outside collaborations & input
  - Increased consultations, links to medical profession and academia, continuing education and mentoring, quality work environment for staff
  - Enhanced communication in review processes
- Strengthen base for CBER science
  - Enhanced interactions and consultation with NIH, other regulatory authorities, and other partners
  - Includes epidemiologic, clinical, and risk sciences

CBER Priority Issues
continued

- New Office: Cells, Tissues and Gene Therapy (OCTGT)
- Implementation of Tissue rules
  - Establishment Registration and Listing (Final, effective 4/4/01)
  - Suitability Determination for Donors (Proposed 1999)
  - Current Good Tissue Practice (Proposed 2001)
    - Proposed rules both nearing final
- Strengthen emergency response/crisis management
  - “Routine” product related
  - Counter-terrorism (CT)

CBER Priority Issues
continued

- Development/availability of biological product countermeasures to CT
- Address emerging infectious diseases (e.g., West Nile, monkeypox, SARS)
- Implement MDUFMA with excellent first year results
- Continue to develop/enhance risk-based strategies

Biologics: Unique Attribute and Risk Issues

- Biologic sources (human/animal communicable diseases)
- Multiple mechanisms of action
- Predictors of toxicity often not established
- Complex manufacturing processes
- Broad range of affected individuals
  - Healthy to elective surgery to severely ill
- Uncertainty
  - For example, emerging infectious disease threats and blood
  - Cutting-edge technology: less experience, more interest

Unique Attribute and Risk Issues
continued

- Products often needed for public health; multiple partners (government & industry)
- Often no substitute product
- Supply and availability as public health issue and factor in risk/benefit assessments
- Acute problems with limited information on product
- High public interest
- Perceived-real needs for immediate action

CBER Roles Relating to Product Testing and Approvals

- Roles:
  - Facilitate product development
  - Facilitate product availability
  - Help assure product integrity
  - Related research and regulatory activity

Approaches to Speed Product Availability and Licensure

- Early and frequent consultation between sponsor and FDA
- Availability for emergency use under IND
- Fast track and accelerated approval process
- Priority review
- Approval under “animal rule”
- Careful attention to risk/benefit and risk management issues
- Incentives (e.g., orphan drugs, new: ???)

Early and Frequent Consultation

- Improves communication process
- Improves quality and efficiency of laboratory and clinical studies
- Reduces misunderstandings and likelihood of unwelcome “surprises,” multiple review cycles
- Improves efficiency of product development
- Very resource intensive for FDA
- Project teams at CBER being used for this purpose (e.g., for priority BT product development and review)

Priority Review

- Product is a significant advance (drugs)
- For serious or life threatening illness (biologics)
- 6 month complete review of license application
- Recent example: pneumococcal conjugate vaccine (Prevnar©)

Fast Track, Accelerated Approval

- Serious/life threatening: meaningful therapeutic benefit over existing Rx
- Allows for rolling submission
- Accelerated approval:
  - Utilize surrogate endpoints for clinical benefit (21 CFR 314.50, subpart H)
  - Post-licensure studies required (usually ongoing) to demonstrate effects on disease outcomes
  - Restrictions on use possible, promotional controls
  - Potential problems obtaining controlled data
- Withdrawal if agreements violated/not safe and effective

General Differences Between CBER and CDER

- CBER regulates biological products under the Public Health Service Act and the Federal Food, Drug, and Cosmetic Act (FDCA)
- CDER regulates drug products under the FDCA
- Biological products (CBER) – derived from living sources, such as humans, animals, plants, and microorganisms

General Differences Between CBER and CDER

continued

- Most biologics (CBER) are complex mixtures that tend to be heat sensitive and open to microbial contamination. So, aseptic principles are used during manufacturing, unlike most conventional drugs
- Most CDER drugs – chemically synthesized and their structure known. CDER regulates prescription drugs, generic drugs, over-the-counter drugs, and now some biological therapeutic drugs

CBER/CDER Therapeutic Product Transfer

- Products involved
- Timeline
- Notification letter
- Web site

Products Involved

- Products That Remain Regulated by CBER
  - Viral-vectored gene insertions (gene therapy)
  - Products composed of human or animal cells or from physical parts of those cells
  - Allergenic products
  - Allergen patch tests
  - Antitoxins, antivenins, and venoms